AMENDMENTS TO THE SPECIFICATION

At page 44, rewrite the first paragraph as follows:

Figure 5 shows the alignment of the amino-acid sequence encoding HDAC1 from man, arabidopsis and yeast. The aligned amino-acid sequences are shown using the one letter code. The sequences in the figure further correspond to SEQ ID No:6 (human HDAC polypeptide); SEQ ID NO:7 (arabidopsis thaliana HDAC polypeptide); and SEQ ID NO:8 (yeast HDAC polypeptide) in the Sequence Listing. The asterisks mark the positions of amino-acids which are identical in all three sequences, whilst the dots show positions of amino-acids which are conservative changes. This alignment is simply meant to illustrate that HDAC genes are present in all eukaryotes from yeast and plants to man and is not an exhaustive list of all known sequences. Note further that a total of six mammalian HDAC genes have been described (see Grozinger *et al* (1999) *Proc. Natl. Acad. Sci. USA* 96, 4868-4873).

Rewrite the paragraph spanning pages 44 and 45 as follows:

Work was carried out to produce an analogue of the PLZF-RARα gene fusion found in acute promyelocytic leukaemia (Guidez *et al* (1998) *Blood* 91, 2634-2642), in which the RARα portion was replaced by an equivalent region of the human estrogen receptor

(ERα). To do this, a 1392 bp region of PLZF coding region was amplified by PCR from a full length cDNA clone using a generic oligonucleotide primer to 5′ flanking cloning vector sequence (T7 primer;) and a primer complementary to PLZF sequences encompassed by bases 1441-1446 of the sequence of Chen *et al* (1993) *EMBO J.* 12, 1161-1167, with additional bases added to the 3′ end, so as to introduce an in-frame XhoI restriction enzyme site (Primer PLZF R; ccgctcgagCTGAATGAGCCAGTAAGTGCATTCTC) (SEQ ID NO:1). Similarly, a 1407 bp region of a human ER RARα cDNA clone (HEG0; Tora *et al* (1989) *EMBO J.* 8, 1981-1986) was amplified by PCR using primers which introduced an in frame XhoI site into 5′ coding region and a BamHI site into the 3′ untranslated region (Primers ER F1; CCGCTCGAGggccaaattcagataatcgac (SEQ ID NO:2) and ER R1; ccgtgtgggaTccagggagctctca (SEQ ID NO:3)). PLZF and ER PCR products were restriction enzyme digested with EcoRI and XhoI and XhoI and BamHI respectively. The digest products were purified and ligated with pSG5 expression vector DNA (Stratagene) previously digested with the restriction enzymes EcoR1 and BamHI. The ligation product was used to transform *E. coli* bacteria and plasmid DNA prepared from individual clones. Recombinant pSG5 plasmids containing PLZF-ER gene fusion DNA were initially identified by restriction enzyme digestion and

were subsequently confirmed by DNA sequence analysis. The resultant cloned PLZF-ER gene encodes the first 455 amino acids of PLZF, fused in frame with amino acids 151-595 of human ERα sequence. This clone was used in experiments to address expression and subsequent inhibition of ER regulated gene activity by the PLZF-ER fusion protein, as shown in Figures 3 and 4.

Rewrite the paragraph spanning pages 48 and 49 as follows:

A second analogue of the PLZF-RARα gene fusion was produced in which the RARα portion was replaced by an equivalent region of the human androgen receptor (AR). A 1146 bp region of a human AR cDNA clone (Tilley *et al* 1989 *Proc. Natl. Acad. Sci. USA* 86, 327-331) was amplified by PCR using primers which introduced an in frame XhoI site into the 5′ coding region and a BamHI site immediately following the stop codon (Primers AR F1, ggagctcgagggTTGGAGACTGCCAGGGACC (SEQ ID NO:4) and AR R1; gtgaggatccTCACTGGGTGTGGAAATAGATGG (SEQ ID NO:5)). The AR PCR product was restriction enzyme digested with XhoI and BanHI and ligated with XhoI/BanHI digested PLZF-ER to replace the ER portion with AR. The ligation product was used to transform *E. coli* bacteria and plasmid DNA prepared from individual clones. Recombinant pSG5 plasmids containing PLZF-AR gene fusion DNA were initially identified by restriction enzyme digestion and

were subsequently confirmed by DNA sequence analysis. The resultant cloned PLZF-AR gene encodes the first 455 amino acids of PLZF, fused in frame with amino acids 537-917 of human AR. Transient transfections in COS-1 cells, followed by immunoblotting of cell extracts with antibodies directed against PLZF or AR were used to confirm expression and expected size.